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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,363	09/06/2005	Kathryn Elizabeth Lawlor	18688	5197

272 7590 02/18/2010

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EXAMINER	
WOODWARD, CHERIE MICHELLE	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,363	LAWLOR ET AL.	
	Examiner	Art Unit	
	CHERIE M. WOODWARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,12,13,22,29-32 and 36* is/are pending in the application.

4a) Of the above claim(s) *22,29-32 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/15/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response filed 10/15/2009 is acknowledged and entered. Claims 6-7, 9-11, 14-21, 23-28, 33-35, and 37-45 have been cancelled by Applicant. Claims 22, 29-32, and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-5, 8, 12, and 13 are under examination.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 10/15/2009 has been considered by the examiner. A signed copy is attached hereto.

Advisory Notice

3. Applicant is advised that the multiple NPL documents submitted in the response filed 10/15/2009 that are not listed on an IDS may not have been considered by the examiner. If Applicant wishes the examiner to fully consider the submitted documents, they must be disclosed on an IDS.

Response to Arguments

Objections/Rejections Maintained

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-5, 8, 12, and 13 remain rejected under 35 U.S.C. 102(e) as being anticipated by Devalaraja et al., US Patent Application Publication 20070059280 (published 15 March 2007, benefit to 20 March 2000), as evidenced by Luross et al., (Immunology. 2001 Aug;103(4):407-16, Abstract only), as well as Meisenberg et al., (Blood 1992 May 1;79(9):2267-72; Abstract Only) and Campbell et al., (J Leukoc Biol. 2000 Jul;68(1):144-50, Abstract Only) (both cited for exemplary purposes in response to Applicant's arguments), for the reasons of record and the reasons set forth herein.

Applicant repeats previously presented arguments and argues that the '280 publication does not enable the method of treating arthritis by administering an inhibitor of G-CSF, including antibodies to G-CSF (Remarks, p. 2). Applicant argues that the specification of the '280 publication is identical to the specification of US Patent 7,108,852 and that the prosecution history of the '852 patent is relevant in the instant case (Remarks, p. 2). Applicant argues that the '852 specification discloses that the antagonist of G-CSF is no greater than the antagonism of M-CSF and that the claims in the '852 patent are drawn to methods of treating arthritis by administering an antibody to M-CSF (Remarks, p. 2). Applicant argues that during the prosecution of the '852 patent, the claims were initially rejected by the USPTO as not being enabled (Remarks, pp. 2-3). Applicant refers to the Office Action mailed 7 April 2004 in 09/885,259 as Exhibit A (Remarks, p. 3). Applicant argues that only subsequent presentation of actual animal data provided sufficient enablement for the claimed subject matter (Remarks, p. 3). Applicant argues that because the '280 publication does not disclose the requisite animal data with respect to the antagonist of G-CSF, the disclosure is not enabling for claims directed to treating arthritis by administration of G-CSF antagonists (Remarks, p. 3). Applicant also argues that there is no justification "of record or anywhere" to distinguish the M-CSF antagonist and the relationship in the treatment of arthritis of the '852 patent from the G-CSF antagonist of the '280 publication (Remarks, p. 3). Applicant also argues that the "uncertainty in this complex field with respect to the antagonism of a single agent could only be overcome by a specific teaches in the accepted animal model" (Remarks, p. 3). In footnote number one, Applicant's argue that the claims are characterized by the transitional phase "consisting of" which distinguishes the plain reading of the '280 publication (Remarks, p. 3, footnote 1). Applicant argues that the methods disclosed in the '280 publication in relation to G-CSF are "merely based on an observation of the synergistic effect of exogenously added G-CSF on chemokine mediated inflammation" (Remarks, p. 3). Applicant also argues that the '280 publication only discloses the potentiating effect of G-CSF on IL-8 mediated chemotaxis (Remarks, p. 3). Applicant submits Exhibit B (Keystone et al., 2003 paper) as evidence that the direct antagonism of IL-8 by the administration of IL-8 Mab has not proven to be effective against rheumatoid arthritis (Remarks, p. 3). In footnote two (2) Applicant states that "those skilled in the art are held to appreciate the unpredictability in the art as well which [sic] is also "old" and unreconciled in the art" (Remarks, p. 3).

Applicant argues that the '280 publication also discloses experimental data which contradict[s] the potentiating effect of G-CSF on IL-8 mediated chemotaxis (Remarks, p. 4). Applicant submits Exhibit C, a Declaration filed under 37 CFR 1.132 by co-inventor Wicks to support the conclusion that the '280 publication is not enabling for a claim directed to a method of treating arthritis by the administration of an

antagonist of G-CSF (Remarks, p. 4). Applicant argues that the '280 publication, taken as a whole, is not enabling for the claimed method of treating arthritis "solely" with an antagonist of G-CSF (Remarks, p. 4).

Applicant's arguments and the Declaration of co-inventor Wicks submitted under 37 CFR 1.132 have been considered, but they are not persuasive.

With regard to Applicant's correlation of the '280 application to the '852 patent and its prosecution history, Applicant's arguments and analogy are misplaced for several reasons. Applicant argues that during the prosecution of the '852 patent, the claims were initially rejected by the USPTO as not being enabled and Applicant refers to the Office Action mailed 7 April 2004 in 09/885,259 as Exhibit A. Applicant's arguments appear to be disingenuous and entirely without merit. If Applicant's representative took the time to look up the prosecution history in the '259 case, he should have reasonably been apprised that the scope of enablement rejection set forth in the Office Action of 4/7/2004 was immediately withdrawn in the very next Office Action (11/22/2004), after the Applicant in that case responded, specifically pointing out support for the claims in the specification at page 15, lines 1-12 of the specification and in the provisional application 60/190842, to which the '852 patent and the '280 publication claim and benefit (see the '259 application Remarks, filed 9/15/2004 and the Office Action mailed 11/22/2004). Applicant's argument that "only a subsequent presentation of actual animal data in well accepted experimental models relative to M-CSF antagonists provided sufficient enablement for the claimed subject matter" is entirely without merit. The Remarks of Applicant in the 9/14/2004 Response and the Declaration submitted therewith, reminded the examiner in the '259 case of Example 1 of the '842 provisional application, to which benefit was accorded in the '259 application. The provisional application recites specific i*n vivo* recruitment experiments with G-CSF (see pages 16-19 and claims 1, 2, 9, and 14). This was pointed out in the Applicant's Response filed on 9/15/2004 and supported by the Declaration submitted therewith. The issued '852 patent claimed and was accorded benefit to the 60/190,842 provisional application and accordingly the teachings and examples in the '842 provisional application are subsumed within and provide enabling support for the subject matter claimed in the '852 patent. This was recognized by the examiner of the '259 application during prosecution and the scope of enablement rejection was withdrawn.

Further, both the provisional 60/190,842 application containing the animal model studies and Example 1, beginning at paragraph 127 of the '280 publication, are applicable to the instant case because the cited '280 publication claims and is accorded benefit to the '842 provisional application and both the '280 publication and the '842 provisional filing teach specific i*n vivo* recruitment experiments with G-

CSF (see pages 16-19 and claims 1, 2, 9, and 14 of the '842 provisional and Example 1, paragraphs 127-134 of the '280 publication) that are sufficient to enable a method of treating arthritis comprising administering an antibody to G-CSF.

As previously stated of record, with regard to Applicant's arguments that the '280 publication does not provide a showing based on an accepted experimental model of arthritis, such a showing is not required where the '280 publication teaches treatment of rheumatoid arthritis by administering antibodies against G-CSF or G-CSFR and the art teaches that collagen-induced arthritis is an accepted animal model of rheumatoid arthritis, as evidenced by the Luross et al., publication, cited of record. Moreover, as stated of record, the '280 publication teaches known models of transgenic and knockout G-CSFR mice (paragraph 3).

Moreover, for Applicant to cite and rely on partial prosecution history in a case that is not presently cited as prior art and then picking and choosing from the prosecution history in that case, without regard for the entire prosecution history, is not beneficial to compact prosecution in the instant case.

Co-inventor Wick's Declaration filed under 37 CFR 1.132 is noted and has been considered, but it is not persuasive. There are multiple co-inventors of the instant invention, yet only one Declaration was submitted. This declaration is not sufficient to manifest an unbiased showing that the cited prior art of record lacks enablement. Moreover, the very prosecution history cited by Applicant demonstrates that enablement was in fact found and accorded, contrary to the assertions and Declaration of Applicant.

As previously argued and responded to of record, Applicant continues to misinterpret the instant claim language where claim 1, for example, uses the transitional phrase "consisting of." The "consisting of" language is proper language for a Markush group, wherein the composition comprises an agent "consisting of" one of the multiple recited embodiments from the Markush group. However, the instant claims are not limited to administration of a G-CSF antibody because the method of claim 1 specifically and plainly recites "said method comprising administering to the subject an effective amount of an agent consisting of…" The comprising language of the method does not further limit other method steps that could be added to the method, including the administration of other polypeptides, small molecules, carriers, pharmaceutical compositions, etc., so long as the administration encompasses at least one of the agents from the recited Markush group. The examiner is required to read the claims in their broadest reasonable interpretation. Accordingly, the claims, as written, do not recite a method of treating arthritis "solely" with an antagonist of G-CSF.

Regarding Applicant's argues that the methods disclosed in the '280 publication in relation to G-CSF are "merely based on an observation of the synergistic effect of exogenously added G-CSF on chemokine mediated inflammation," Applicant's arguments are contradicted by the data and experimental models of the '280 publication and provisional application to which it claims benefit. Moreover, Applicant should be well aware that autoimmune disorders, including arthritis, do not occur *in vivo* in a vacuum. Multiple factors drive immune responses and additive and synergistic effects drive immune responses, be they "normal" or aberrant responses.

Regarding Applicant's argument that the '280 publication only discloses the potentiating effect G-CSF on IL-8 mediated chemotaxis, Applicant's attention is drawn to Figure 5, which shows that G-CSF enhances *in vivo* neutrophil intradermal recruitment. Figure 7 shows that G-CSF neutralizing antibodies inhibit G-CSF synergized chemotaxis of neutrophils. This inhibition is important in treating arthritis involving aberrant neutrophil recruitment, for example in the arthritis of Familial Mediterranean Fever and rheumatoid arthritis.

Applicant's journal publication Exhibits are noted, but they are not persuasive. As stated above, autoimmune disorders, including arthritis, do not occur *in vivo* in a vacuum. Multiple factors drive immune responses and additive and synergistic effects drive immune responses, be they "normal" or "aberrant" responses. Inhibition of IL-8 by IL-8 monoclonal antibodies in the treatment of rheumatoid arthritis is not the subject of the claims of the instant application. Instead, the instant claims are drawn to a method of treating generic arthritis, including one embodiment of rheumatoid arthritis, and one embodiment of collagen-induced arthritis, comprising administering an antibody to G-CSF or G-CSFR, etc. Accordingly, the Keystone et al., (2003) reference is not on point with the instant claims.

As stated of record, Applicant is reminded that a composition and its properties are inseparable and that the art clearly shows that both endogenously administered G-CSF and exogenously administered G-CSF have the same effect of driving bone marrow granulocyte production. Accordingly, treatment of arthritis where there is a prevalence of granulocytes (*i.e.* neutrophils), would be affected by administering a G-CSF antibody or G-CSFR antibody to block granulocyte production or function, as taught by the '280 publication. The '280 publication need not teach what is old and well known in the art in order to be enabled. The fact that the '280 publication does discuss what is well known in the art is sufficient for the disclosure of the '280 publication to meet the requirements of 35 USC 112, first paragraph.

As previously stated of record, with regard to Applicant's argument directed to the synergistic effect of exogenously added G-CSF, Applicant focuses its argument on only one alternative embodiment of the '280 publication. Applicant's attention is drawn to paragraphs 33-43 where the method of *in vivo*

treatment is directed to treatment of inflammation caused by endogenous mediators. Treatment of rheumatoid arthritis is specifically discussed in paragraph 42 and "especially preferred inhibitors" are monoclonal antibodies to G-CSF or G-CSFR (paragraph 32).

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/

Primary Examiner, Art Unit 1647